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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/462,909	02/14/2000	ANNIE MEINIEL	065691/0179	5643

7590 10/18/2002

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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 10/18/2002

18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/462,909	MEINIEL ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-24 is/are pending in the application.

4a) Of the above claim(s) 2-4,7,9,10,12,14,15,18,19, 21,23, 24 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,5,6,8,11,13,16,17,20 and 22 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the claims

1. Claims 1-5 and 7 have been amended and claims 16-24 have been added as requested in the amendment of Paper No. 16. Claims 1-24 are pending in the instant application.

Election/Restrictions

2. Applicant's election with traverse of Group III in Paper No. 12 and election of SEQ ID NO: 7 as a single molecular embodiment for examination in Paper No. 16 is acknowledged. The traversal is on the ground(s) that restriction between Group III and Group V is not proper because special technical feature of Group I, a protein of SEQ ID NO: 1 is the same as in Group V directed to DNA encoding a protein of SEQ ID NO: 1. This is not found persuasive because pursuant to 37 C.F.R. § 1.475 (d), the ISA/US considers that where multiple products and processes are claimed, the main invention shall consist of the first invention of the category first mentioned in the claims and the first recited invention of each of the other categories related thereto. Accordingly, the main invention (Group I) comprises the first recited product, a protein of SEQ ID NO: 1 (claims 1-8), and a first method of use of the protein, which is a method for regenerating nervous system cells by contacting the cells with the protein of SEQ ID NO: 1 (claim 9). Pursuant to 37 C.F.R. § 1.475 (d), the ISA/US considers that any feature which is the subsequently recited products and methods share with the main invention does not constitute a special technical feature within the meaning of PCT Rule 13.2 and that each of such products and methods accordingly defines a separate invention.

However, in the instant case, according to the search report (see document A5 of IDS, Paper No. 4), a protein comprising SEQ ID NO: 8, which is a species sequence of SEQ ID NO: 1, was known in prior art before the instant invention was made. Therefore, it cannot serve as a unifying special technical feature. The "special technical features" means those technical features that define a contribution over the prior art. (See M.P.E.P. 1850.) Thus, the apparent "special technical feature" of these claims cannot form the basis of unity of invention, and, therefore, further restriction within the elected Group III to one of the following inventions is required under 35 U.S.C. 121:

Claims 1, 5, 6, 8, 13, 16, 17 and 22, in so far as they are directed to a peptide of SEQ ID NO: 7 or SEQ ID NO: 8, classified in class 530, subclass 300, for example.

Claims 11, 20, in so far as they are directed to a method of treatment by administration of a peptide of SEQ ID NO: 7 or 8, classified in class 514, subclass 2, for example.

The inventions are distinct, each from each other because of the following reasons:

Inventions of claims 1, 5, 6, 8, 13, 16, 17 and 22 and claims 11 and 20 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the peptides of claims 1, 5, 6, 8, 13, 16, 17 and 22 could be used in an entirely different manner such as for the production of antibodies rather than in the method of claims 11 and 22.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, recognized divergent subject

matter and non-coextensive literature searches, restriction for further examination purposes as indicated is proper.

Applicant is advised that the reply to this office action to be complete must include an election of the invention to be further examined even though the requirement be traversed (37 CFR 1.143).

In case the election between two groups of claims is made without traverse, Applicant is only required to respond to the part of the office action, which refers to the examination of the elected claims and not to whole text of the office action.

3. Originally elected Group III consists of claims 1-8, 11, 13 and newly added claims 16-17, 20 and 22. Additionally, because Applicant elected SEQ ID NO: 7 as a single molecular embodiment of the peptide for examination (see last paragraph of Paper No. 16) and because SEQ ID NO: 8 is a representative sequence that encompasses SEQ ID NO: 7, the claims that include SEQ ID NO: 8 are also included in the examination.

Claims that read on the peptides of SEQ ID NOS: 7 and 8 are as follow: claims 1, 5, 6, 8, 11, 13, 16, 17, 20 and 22.

Claims 2-4, 7, 9-10, 12, 14-15, 18-19, 21 and 23-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12.

Claims 1, 5, 6, 8, 11, 13, 16, 17, 20 and 22 in so far as they are directed to SEQ ID NOS: 7 and 8 are under examination in the instant office action.

Priority

4. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in France on 07/16/1997. It is noted, however, that applicant has not filed a certified copy of the 97/09016 application as required by 35 U.S.C. 119(b).

Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a translation of the foreign application should be submitted under 37 CFR 1.55 in reply to this action.

5. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). If the application claims the benefit of an international application, the first sentence of the specification must include an indication of whether the international application was published under PCT Article 21(2) in English (regardless of whether benefit for such application is claimed in the application data sheet).

Specification

6. It is noted that the instant specification is not in compliance with the requirements for Sequence Identifiers (see MPEP 2422.03). See, for example, page 2 of the instant specification. The proper format to present a sequence is by identifying it by SEQ ID NO: X. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 1, 5, 6, 16, are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims fail to include any limitations, which would distinguish the claimed proteins, peptides and compositions from those, which occur in nature. In the absence of the hand of man, naturally occurring nucleic acid molecules and proteins are considered non-statutory subject matter. Diamond v. Chakrabarty, 206 USPQ 193 (1980). Additionally, mere purity of a naturally occurring product does not necessarily impart patentability. Ex parte Siddiqui, 156 USPQ 426 (1966). However, when purity results in a new utility, patentability is considered. Merck Co. v. Chase Chemical Co., 273 F. Supp. 68 (1967). Filing of evidence of a new utility imparted by the increased purity of the claimed invention and amendment of the claims to recite a purity limitation, if supported by the specification, is suggested to obviate this rejection. Applicant should point to the basis in the specification for any amendment to the claims.

8. Claims 1, 5, 6, 8, 13, 16, 17 and 22 are further rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant application has provided a description of a protein. The instant application does not disclose the biological role of this protein or its significance.

It is clear from the instant application that the protein described therein is what is termed an "orphan protein" in the art. The DNA of the instant application has been isolated because of its similarity to a known DNA. There is little doubt that, after complete characterization, this DNA and encoded protein may be found to have a specific and substantial credible utility. This

further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion".

The instant claims are drawn to peptides of as yet undetermined function or biological significance. It is stated in the instant specification that "a novel peptide, which is active in the regeneration of the nervous system" has a structural similarity to "one of the TSRs [thrombospondin type I units] of SCO-spondin" (page 2, lines 9-15 of the instant specification). It is also stated that TSRs "have highly varied activities depending on the biological system in which they are involved" (page 1, lines 11-14). More specifically, the biological properties of some synthetic peptides deduced from TSR units include "the adhesion of the plasmodium sporozoites to the hepatic cells, [...] cellular attachment in other biological models", and also binding heparin and certain growth factors (page 1, lines 29-35). Therefore, based on the

structural similarities to different known proteins with certain function, it has been suggested that the peptides of the instant invention would also possess similar biological activity. Numerous publications exist on a topic of predicting protein functions from structural similarities or homology to the known proteins. It is well described in the art that amino acid structure cannot necessarily predict the function of the protein: "Knowing the protein structure by itself is insufficient to annotate a number of functional classes and is also insufficient for annotating the specific details of protein function" (see Skolnick et al., Box 2 on page 36 and the whole paper). Moreover, "Structural similarity does not necessarily mean a common evolutionary origin and homologous sequences may evolve into different folds (according to current classification schemes) (See Bork et al., Current Opinion in structural Biology, 1998, 8, page 332, first column, second paragraph). Thus, according to the state of the art, functional characteristics of a protein cannot be unequivocally extrapolated from its structural characteristics.

In the absence of knowledge of the biological significance of these specific peptides, there is no immediately obvious patentable use for the claims proteins. According to the specification of the instant application "[I]n the presence of the peptide SEQ ID NO: 8, the neurons aggregate and are essentially connected by bundles of long and thick neurites after 5 days in culture " (page 9, lines 32-35 of the instant specification). The instant specification fails to provide any evidence or sound scientific reasoning that would support a conclusion that the aggregation of neurons treated with a peptide of SEQ ID NO: 8 in culture is associated with regeneration of nervous system. Based on the data provided in Examples 1 and 2, one skilled in the art would not reasonably believe that the effect of the peptide of SEQ ID NO: 8 on adhesion of the cultured cells to the plastic surface of the tissue flasks, can be directly connected with "the

growth of the neurons" (page 8, line 5). There is no information presented in the instant specification, or known in the prior art that would support a nexus between increase in neuronal adhesion and the ability of neuronal revival or regeneration. One would not rationally expect that administration of a peptide of SEQ ID NO: 8 to an individual suffering from pathological condition or trauma, which requires regeneration of nervous system cells, would cause any effect because the biological role of the claimed peptide is not yet determined.

Moreover, according to the results obtained from the experiments using NIB104 cells, "[i]n the presence of the peptide SEQ ID NO: 8 [...] NIB104 neuroblastoma cells are considerably less numerous than in the control cultures" (page 12, lines 5-8). Thus, treatment of neuronal cells with a peptide of SEQ ID NO: 8 appears to lead to a decrease in neuronal survival or suppressed proliferation of neuronal cell line cells.

Because the instant specification does not teach a biological activity of the protein, which supports a practical utility, one would not reasonably believe that the administration of the claimed peptide would prevent or treat a condition or disease, like regeneration of nervous system cells or for treating a neurodegenerative disease, as implied by the specification. To employ a nucleic acid of the instant invention in any of the disclosed methods would clearly be using it as the object of further research, which has been determined by the courts to be a utility, which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for the encoded protein then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 5, 6, 8, 13, 16, 17 and 22 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

10. Claims 1, 5, 6, 8, 11, and 13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 recites the limitations of SEQ ID NO: 15-20, which are not supported by the instant specification and were not present in the originally filed PCT/FR98/01556. Claims 5, 6, 8, 11 and 13 depend from claim 1. Therefore, it is concluded that the recitation of peptides of SEQ ID NOS: 15-20 in claim 1 introduces new matter into the claims 1, 5, 6, 8, 11 and 13.

11. Claims 11 and 20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 11 and 22 are directed to a method for treating a pathological condition or trauma requiring the regeneration of nervous system cells by administration of a peptide of SEQ ID NO:

7 or SEQ ID NO: 8. The instant specification fails to provide enough guidance that would enable one skilled in the art to practice the claimed method without undue experimentation.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. In re Wands, 8 USPQ2d, 1400 (CAFC 1988).

The state of the art on the topic of regeneration of neuronal tissue is very unpredictable. For example, "it is well-established fact that long nerve fiber pathways do not regenerate in the adult mammalian central nervous system" (Hoffer et al., 1997, J. Neural Transm, 49, pp.1-10). Moreover, because biological function of peptides of SEQ ID NO: 7 and 8 is unknown, one would not expect that administration of these peptides would lead to regeneration of nervous system cells (see reasons of record in section 8 of the instant office action).

The standard of an enabling disclosure is not the ability to make and test if the invention worked but one of the ability to make and use with a reasonable expectation of success. To practice such a method would require knowledge of the route, duration and quantity of administration of the peptides of SEQ ID NO: 7 or 8 to a subject and this information is not provided by the instant specification. The text of the instant specification clearly fails to supply the guidance that would be needed by a routine practitioner to successfully conduct such a treatment. The instant specification has also failed to disclose how these parameters are to be determined, how a similar method was practiced in the art with a different agent or to provide

even a single working example, prophetic or actual, of the claimed method. In the absence of this guidance a practitioner would have to resort to a substantial amount of undue experimentation involving the variation in the amount and duration of administration of peptides of the instant invention and in determining a suitable route of administration. The instant situation is directly analogous to that which was addressed in *In re Colianni*, 195 U.S.P.Q. 150,(CCPA 1977), which held that a "[d]isclosure that calls for application of "sufficient" ultrasonic energy to practice claimed method of fusing bones but does not disclose what "sufficient" dosage of ultrasonic energy might be or how those skilled in the art might select appropriate intensity, frequency, and duration, and contains no specific examples or embodiment by way of illustration of how claimed method is to be practiced does not meet requirements of 35 U.S.C. 112 first paragraph".

In view of the lack of teachings and unpredictability of the art set forth earlier, and also the total absence of the working examples, the instant specification is not found to be enabling for a method for treating a pathological condition or trauma requiring regeneration of nervous system. It would require undue experimentation and making a substantial inventive contribution for the skilled artisan to discover how to use Applicants' invention as currently claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1, 5, 6, 8, 11, 13, 16, 17, 20 and 22 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claim 1 is vague and indefinite because it is not clear how to select 1 to 5 amino acids from the group consisting of SEQ ID NOS: 25-49. Is it selection of any amino acid from these sequences or is A_1 and A_2 are selected from the group consisting of SEQ ID NOS: 25-49? Also, the limitation "with the exception of the peptides" is confusing because it can be applied either to a peptide of SEQ ID NO: 1 or to the selection of A_1 and A_2. Clarification is required.

14. Claims 5 is vague and ambiguous for recitation "and 89-96". The metes and bounds of the recitation cannot be determined from the claim.

15. Claims 5, 6, 8, 13, 16, 17 and 22 are indefinite for being dependent from indefinite claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1, 5, 6, 8, 13, 16, 17 and 22 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Gobron et al. (J. Cell Sci, 1996, 109, pp.1053-1061, reference A5 of the IDS of Paper No. 4). Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claims 1, 5, 6, 8, 13, 16, 17, 22 are directed to a peptides comprising amino acid sequence of SEQ ID NOS: 1, 7 and 8, pharmaceutical compositions and additives for culturing nerve cells comprising such peptides. Document of Gobron et al. discloses a fragment of SCO-

spondin, which has the amino acid sequence identical to SEQ ID NO: 8 of the instant application and also matches the description of SEQ ID NO: 7 and 1, thus, meeting the limitations of claims 1, 5, 6 and 16 (see a copy of the printout of the sequence alignment attached to the instant office action). Moreover, the SCO-spondin of Gobron et al. was used in a culture media for the primary cultures of the neuronal cells (see page 1054 of A5 document, second column, third paragraph), which meets the limitations of claims 8, 13, 17 and 22.

Conclusion

17. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original

signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D.
October 17, 2002

JOHN ULM
PRIMARY EXAMINER
GROUP 1800